Feverfew: Mechanisms of Action and Clinical Efficacy for Migraines and Arthritis

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Feverfew - Mechanisms of Action and Clinical Efficacy for Migraine Prophylaxis

Randomised double-blind placebo-controlled trial of feverfew in migraine prevention.

Murphy JJ, Heptinstall S, Mitchell JR. 88 Jul 23;2(8604):189-92. Lancet. 1988 Jul 23;2(8604): 189-92. Department of Medicine, University Hospital, Nottingham.

Abstract

The use of feverfew (Tanacetum parthenium) for migraine prophylaxis was assessed in a randomised, double-blind, placebo-controlled crossover study. After a one-month single-blind placebo run-in, 72 volunteers were randomly allocated to receive either one capsule of dried feverfew leaves a day or matching placebo for four months and then transferred to the other treatment limb for a further four months. Frequency and severity of attacks were determined from diary cards which were issued every two months; efficacy of each treatment was also assessed by visual analogue scores. 60 patients completed the study and full information was available in 59. Treatment with feverfew was associated with a reduction in the mean number and severity of attacks in each two-month period, and in the degree of vomiting; duration of individual attacks was unaltered. Visual analogue scores also indicated a significant improvement with feverfew. There were no serious side-effects.

Efficacy of feverfew as prophylactic treatment of migraine.

Johnson ES, Kadam NP, Hylands DM, Hylands PJ.
Br Med J (Clin Res Ed). 1985 Aug 31;291(6495):569-73.

Abstract

Seventeen patients who ate fresh leaves of feverfew daily as prophylaxis against migraine participated in a double blind placebo controlled trial of the herb: eight patients received capsules containing freeze dried feverfew powder and nine placebo. Those who received placebo had a significant increase in the frequency and severity of headache, nausea, and vomiting with the emergence of untoward effects during the early months of treatment. The group given capsules of feverfew showed no change in the frequency or severity of symptoms of migraine. This provides evidence that feverfew taken prophylactically prevents attacks of migraine, and confirmatory studies are now indicated, preferably with a formulation controlled for sesquiterpene lactone content, in migraine sufferers who have never treated themselves with this herb.

The therapeutic activity of feverfew on migraines and epilepsy may be due to its GABA-benzodiazepine modulatory effects.
GreenMedInfo Summary

Abstract Title: Bioassay-guided isolation of apigenin with GABA-benzodiazepine activity from Tanacetum parthenium.

A K Jäger, H B Rasmussen, K Krydsfeldt. Phytother Res. 2009 Nov;23(11):1642-4. PMID: 19441011

Abstract

Extracts of Tanacetum parthenium are used in the prophylactic treatment of migraine and have also been used in Danish folk medicine for the treatment of epilepsy. An ethanol extract of T. parthenium showed high affinity for the GABA(A)-benzodiazepine site. An ethanol extract of T. parthenium was fractionated by VLC on silica and preparative C18 HPLC. Each step was monitored with the GABA(A)-benzodiazepine bioassay. The fractionation led to the isolation of apigenin, which may be responsible for CNS-effects of T. parthenium extracts.

The efficacy and safety of feverfew (Tanacetum parthenium L.): An update of a systematic review.

Ernst E, Pittler MH. Public Health Nutr. 2000 Dec;3(4A):509-14.
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Abstract

OBJECTIVE:
Feverfew (Tanacetum parthenium L.) is a popular herbal remedy often advocated for the prevention of migraine. The aims of this systematic review are to update the evidence from rigorous clinical trials for or against the efficacy of feverfew for migraine prevention and to provide a safety profile of this herbal remedy.

DESIGN:
Literature searches were performed using the following databases: Medline, Embase, Biosis, CISCOM and the Cochrane Library (all from their inception to December 1999). Only randomized, placebo-controlled, double-blind trials of feverfew mono-preparations for the prevention of migraine in human subjects were included. All articles were read by two independent reviewers. Data were extracted in a pre-defined, standardized fashion. The methodological quality of the trials was evaluated by the Jadad score. For the assessment of safety issues, major reference texts were also consulted.

RESULTS:
Six trials met the inclusion/exclusion criteria. The majority favour feverfew over placebo. Yet important caveats exist. The data also suggest that feverfew is associated with only mild and transient adverse effects and few other safety concerns.

CONCLUSIONS:
Feverfew is likely to be effective in the prevention of **migraine**. There are no major safety problems.

Gene response of human monocytic cells for the detection of anti-migraine activity of feverfew extracts.

Chen CF, Leung AY. Can J Physiol Pharmacol. 2007 Nov;85(11):1108-15. Source - Department of Genetics and Biochemistry, Jordan Hall 100, Clemson University, Clemson, SC 29634, USA. cchen@clemson.edu

Abstract

The herb feverfew is a folk remedy for various conditions, including inflammation, fever, psoriasis, rheumatism, and asthma. Like many herbal medicines, feverfew's mechanisms of action in the human body are largely unknown and its active ingredients remain elusive. Very often, different extraction methods of herb material produce different physical and biochemical properties and variation in clinical efficacy. We identified 3 major methods of extraction for feverfew aerial parts and used microarray technology to test the hypothesis that extracts produced by different methods elicit different gene expression profiles. We have identified approximately 200 genes that are consistently regulated by the 2 presumptive active anti-migraine feverfew extracts but not associated with the inactive extract. Our results suggest that the presumptive active feverfew extracts potently stimulate more genes in human cells than the inactive extracts. We also identified several genes as unique signatures for these active extracts. All 3 feverfew extracts exhibited similar blockades on lipopolysaccharide-mediated TNF-alpha (tumor necrosis factor alpha) release, implicating that TNF-alpha is not responsible for the differences in the effects of the 3 feverfew extracts in human cells. In contrast, the active extracts more effectively suppressed CCL2 (also known as monocyte chemoattractant protein 1, MCP-1) than the inactive extracts, suggesting that CCL2 is a potential cellular target for feverfew's anti-migraine effects

Application of NFkappaB inhibitor for arthritis.

Tomita T, Kunugiza Y, Nomura K, Morimoto D, Kuroda S, Yoshikawa H

Nihon Rinsho Meneki Gakkai Kaishi. 2009 Apr;32(2):71-6.

Department of Orthopaedics, Osaka University Graduate School of Medicine.

Abstract

Recent progress in DNA technologies has provided the strategies to regulate the transcription of disease-related genes in vivo using antisense oligodeoxynucleotide (ODN). Transfection of cis-element double-stranded oligodeoxynucleotides (decoy ODNs) has been reported as a new therapeutic tool of anti-gene strategies for gene therapy. In the field of arthritis, decoy ODNs strategies have been significant therapeutic potential. In vitro studies demonstrated that the inhibitory effect on inflammatory cytokines and matrix The concept of regulation the disease related gene expression at the level of transcriptional factor may be more therapeutic effects compared with monotherapy in arthritis. Injection of NFkappaB decoy ODN into the affected joint resulted in marked suppression of joint destruction in CIA models.metalloproteinase production from stimulated synovial cells derived from rheumatoid arthritis patients. NFkappaB decoy ODN inhibited induction of osteoclasts and bone resorption ability. Parthenolide is one of the main sesquiterpense lactones responsible for the bioactivities of feverfew and recently reported to inhibit NFkappaB activation. Parthenolide has ameliorated the severity of joint destruction in experimental animal model. Based upon these findings, NFkappaB may be one of important therapeutic target for arthritis.

Inhibition of 5-lipoxygenase and cyclo-oxygenase in leukocytes by feverfew. Involvement of sesquiterpene lactones and other components.

Sumner H, Salan U, Knight DW, Hoult JR. Pharmacology Group, King's College London, U.K. Biochem Pharmacol. 1992 Jun 9;43(11):2313-20

Abstract

Leaves or infusions of feverfew, Tanacetum parthenium, have long been used as a folk remedy for fever, arthritis and migraine, and derived products are widely available in U.K. health food shops. Previous reports have suggested interactions with arachidonate metabolism. Crude chloroform extracts of fresh feverfew leaves (rich in sesquiterpene lactones) and of commercially available powdered leaves (lactone-free) produced dose-dependent inhibition of the generation of thromboxane B2 (TXB2) and leukotriene B4 (LTB4) by ionophore- and chemoattractant-stimulated rat peritoneal leukocytes and human polymorphonuclear leukocytes. Approximate IC50 values were in the range 5-50 micrograms/mL, and inhibition of TXB2 and LTB4 occurred in parallel. Isolated lactones (parthenolide, epoxyartemorin) treated with cysteine (to neutralize reactive alpha-methylene butyrolactone functions of the sesquiterpenes). Inhibition of eicosanoid generation appeared to be irreversible but not time-dependent. We conclude that feverfew contains a complex mixture of sesquiterpene lactone and non-sesquiterpene lactone inhibitors of eicosanoid synthesis of high potency, and that these biochemical actions may be relevant to the claimed therapeutic actions of the herb.